immortalized" in claims 1, 6-8 and 23 is unclear. In addition, the Examiner believes that claim 1 fails to identify what constitutes first and second growth media.

Applicants respectfully traverse this ground for rejection. Within the specification, Applicants have defined "conditionally-immortalized" cells as referring to cells that are transfected with a gene that promotes growth of the transfected cell, such that the production and/or activity of the growth-promoting protein is regulatable by an external factor and suppression of the growth-promoting protein results in differentiation of the cells (*see* page 5, lines 20-24, and page 8, lines 4-7, of the specification). Applicants believe that this definition is consistent with the common understanding of the term "conditionally-immortalized," and that the subject matter encompassed by the claims would be apparent to those of ordinary skill in the art. Nonetheless, to clarify this point, Applicants have amended claims 1 and 6 to recite that the conditionally-immortalized cells express a growth-promoting protein that is regulated by an external factor, such that suppression of the growth promoting protein results in differentiation of the cell into neurons. Support for this amendment may be found, for example, at page 5, lines 23-24, and page 8, lines 4-7, of the specification as filed. Accordingly, Applicants submit that this ground for rejection has been overcome.

With regard to the Examiner's concerns as to what constitutes first and second growth media, Applicants submit that the present teaching is sufficient to permit those of ordinary skill in the art to employ a variety of media in the practice of the present invention. The first medium may be any standard medium that permits proliferation of the cells (*see* page 5, lines 12-15). The second medium is a medium that permits attachment and proliferation after transfection, and does not contain serum (see page 7, lines 10-19). Many such media are known in the art and Applicants submit that the claims as filed are sufficiently clear on this point. Nonetheless, to facilitate allowance, Applicants have amended claim 1 to recite that the second growth medium is serum-free. Support for this amendment may be found, for example, at page 7, lines 14-19, of the specification as filed. Thus, Applicants submit that this ground for rejection has been overcome.

Claims 1-15 and 23-24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Hoshimaru et al. (*Proc. Natl. Acad. Sci. 93*:1518-1523, 1996) and Prasad et al. (*In Vitro Cell Dev. Biol. 30A*:596-603, 1994), in view of Boss et al. (U.S. Patent No. 5,411,883) and Gallyas et al. (*Neurochemical Research 22*:569-575, 1997). In

particular, the Examiner believes that Hoshimaru et al. disclose immortalized rat neuronal progenitor cells wherein expression of v-myc is driven by a tetracycline-controlled transactivator and a human cytomegalovirus (CMV) promoter, as well as the culturing and selection of the cells on polyornithine/laminin-coated plates, and the use of cytokines, forskolin or growth factors for differentiation. The Examiner believes that Prasad et al. disclose the isolation of an immortalized dopamine-producing nerve cell line derived from fetal rat mesencephalic tissue transfected with an oncogene. The Examiner notes that Hoshimaru et al. and Prasad et al. do not teach the immortalization of human neuronal precursor cell that is capable of differentiating into a dopaminergic and/or GABA-ergic neurons. However, the Examiner believes that Boss discloses the isolation and culture methods for the proliferation of human mesencephalon neuron progenitor cells to produce dopamine-producing cells, and that Gallyas discloses characterization of mouse immortalized neuronal cells. The Examiner believes that it would have been obvious to modify the teachings of Hoshimaru et al. and Prasad et al. with substitution of human mesencephalon neuron progenitor cells as taught by Boss et al. The Examiner further believes that it would have been obvious to characterize immortalized human mesencephalon cells as described by Gallyas et al. because dopamine and GABA are neurotransmitters of interest.

Applicants respectfully traverse this ground for rejection. Hoshimaru et al. describe the generation of conditionally-immortalized cell lines from adult rat neural progenitor cells. Prasad et al. is directed to the generation of immortalized clonal dopamine-producing nerve cells. Applicants agree with the Examiner that Hoshimaru et al. and Prasad et al. do not teach the immortalization of a human neuronal precursor cell that is capable of differentiating into a dopaminergic and/or GABA-ergic neurons. Accordingly, the Examiner's rejection hinges on the disclosure of human mesencephalon neuronal progenitor cells by Boss et al.

Applicants respectfully submit that Boss et al. do not teach or suggest the progenitor cells of the present invention. Boss et al. describe mesencephalon neuron progenitor cells that are prepared so as to permit growth in aggregate cultures (*see* column 3, lines 30-34). The cells of Boss et al. appear to be incapable of forming a true monolayer. The "monolayer cultures" referred to at column 5, line 61 – column 6, line 12 display interconnected three-dimensional structures, rather than the two-dimensional structure characteristic of monolayers (*see* Boss et al., column 6 lines 4-12). In contrast, the cells of the present invention grow strictly

as two-dimensional monolayer cultures, and do not grow as aggregates. To clarify this distinction, Applicants have amended claims 1 and 6 to recite that the cells proliferate as adherent monolayers. Support for this amendment may be found, for example, in the specification at page 7, line 22 and within Figure 1A. Accordingly, Boss et al. do not teach or suggest progenitor cells that satisfy the requirements of claim 6, or that are prepared according to the method of claim 1.

Gallyas et al. do not remedy this deficiency. Gallyas et al. is directed to the use of neurotransmitter concentrations in the characterization of neuronal cell lines. This reference provides no suggestion of human mesencephalon neuronal progenitor cells. Accordingly, Applicants submit that the cited references, alone or in combination, do not teach or suggest the conditional immortalization of a human neuronal precursor cell that is capable of differentiating into a dopaminergic and/or GABA-ergic neurons.

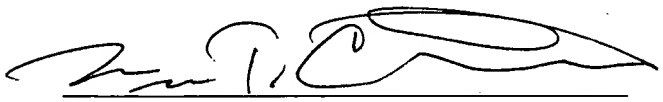
Applicants further wish to point out that those of ordinary skill in the art would not have expected the method of Hoshimaru et al. to permit the immortalization of mesencephalon neuron progenitor cells. Cells from different regions of the CNS are known to respond differently to attempts to generate immortalized cell lines. Prior to the present invention, those of ordinary skill in the art would have had no basis for determining which elements of the Hoshimaru et al. method to retain, and which to alter, for use with mesencephalon neuron progenitor cells. Accordingly, Applicants respectfully submit that this ground for rejection has been overcome.

Applicants are of the belief that all outstanding issues have been addressed and hence the claims are now allowable. Favorable consideration and a Notice of Allowance are

earnestly solicited. If the Examiner does not believe the claims are allowable for any reason, the Examiner is encouraged to telephone the undersigned attorney at (206) 622-4900.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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